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Research Progress on the Anti-Caries Potential of Citrus Reticulata Leaf Fermented Tea Extracts

Juxian Wu *, Huiqing Liu, Xuexun Chen and Xiaorong Wu

Guangdong Polytechnic of Science and Trade, Guangzhou, Guangdong, China

*** Corresponding author:** Juxian Wu (Email: wujuxian2002@163.com)

Abstract: This review summarizes the latest research advancements regarding the anti-caries potential of Citrus reticulata leaf fermented tea extracts. Initially, it introduces the fundamental components and biological activities of Citrus reticulata leaves and fermented tea. Subsequently, the focus shifts to analyzing the mechanisms by which these extracts inhibit cariogenic bacteria, slow plaque formation, and promote tooth mineralization. By integrating recent in vitro studies, animal models, and clinical research, we explore the potential and application prospects of Citrus reticulata leaf fermented tea extracts as natural anti-caries agents. Finally, the review identifies current research limitations and future directions, providing theoretical support and practical guidance for the application of Citrus reticulata leaf fermented tea extracts in oral health.

Keywords: Citrus Reticulata; Fermented Tea; Anti-caries; Oral Health; Cariogenic Bacteria; Dental Plaque; Natural Extracts.

1. Introduction

Dental caries, commonly referred to as tooth decay, is recognized as one of the most prevalent oral diseases globally, significantly impacting the quality of life and health of affected individuals. According to recent epidemiological data, dental caries affects approximately 29.4% of the global population, with high prevalence rates particularly noted among children and adolescents [1]. The disease is characterized by the demineralization of dental enamel due to acid production by cariogenic bacteria, leading to the formation of cavities. If left untreated, dental caries can result in severe complications, including tooth loss and systemic health issues, thereby necessitating effective preventive and therapeutic strategies [2]. The burden of dental caries is substantial, contributing to significant disability-adjusted life years (DALYs) and highlighting the urgent need for innovative approaches to combat this widespread health challenge [3].

Traditional preventive methods for dental caries, such as fluoride applications and mechanical cleaning, have been widely employed. However, these strategies often come with limitations, including potential side effects and issues related to patient compliance [4]. Moreover, the effectiveness of these conventional methods can be variable, depending on individual patient factors and socioeconomic conditions. As such, there is a growing interest in exploring alternative preventive measures that leverage the natural bioactive properties of plant extracts. In particular, natural products have gained attention due to their rich bioactivity and lower toxicity compared to synthetic agents, making them promising candidates for caries prevention [5].

Among various natural products, the leaves of Citrus reticulata (commonly known as tangerine) have emerged as a focal point of research due to their rich composition of flavonoids and essential oils, which exhibit notable antibacterial and anti-inflammatory properties [6]. These bioactive compounds have shown potential in inhibiting the growth of cariogenic bacteria, thereby reducing the risk of dental caries. The use of Citrus reticulata leaves in the form of fermented tea extracts represents an innovative approach to enhancing oral health. The fermentation process not only preserves the beneficial properties of the plant but also enhances the bioavailability of its active components, potentially increasing their effectiveness in preventing dental caries [7].

The process of co-fermentation, where multiple microorganisms are utilized to ferment the tea, can further amplify the health benefits of the resulting extract. By promoting a favorable oral microbiome environment, co-fermented tea extracts may inhibit the growth of harmful bacteria while supporting the proliferation of beneficial species. This bi-directional approach to oral health management aligns with the emerging paradigm of biointervention strategies, which aim to restore the natural balance of the oral microbiota rather than indiscriminately eradicating microbial populations [5]. Thus, the exploration of Citrus reticulata leaf co-fermented tea extracts offers a novel avenue for the prevention of dental caries, with the potential to improve patient outcomes and enhance overall oral health.

This review aims to systematically summarize the current research progress regarding the use of Citrus reticulata leaf co-fermented tea extracts in caries prevention. By analyzing the underlying mechanisms of action and evaluating the application potential of these extracts, this article seeks to contribute to the growing body of knowledge surrounding natural preventive strategies for dental caries. Ultimately, the findings may inform future research directions and clinical practices aimed at reducing the burden of dental caries globally.

2. Main Body

2.1. Analysis of the Components and Biological Activity of Citrus Red Leaf and Co-fermented Tea

2.1.1. Main Chemical Components and Biological Activity of Citrus Red Leaf

Citrus red leaf, known for its rich composition of flavonoids, essential oils, and polyphenolic compounds, serves as a valuable resource in the field of oral health,

particularly in the prevention of dental caries. Flavonoids such as hesperidin and naringin, along with volatile compounds like limonene and citral, contribute significantly to the antimicrobial properties of citrus red leaf extracts. These compounds exhibit potent antibacterial, antioxidant, and anti-inflammatory activities, which are crucial for combating oral pathogens associated with tooth decay. Research has demonstrated that extracts from citrus red leaf can effectively inhibit the growth of Streptococcus mutans, a primary bacterium implicated in dental caries. The antibacterial effects are attributed to the ability of these bioactive compounds to disrupt bacterial cell membranes and interfere with metabolic processes, thereby reducing the viability of cariogenic bacteria. Furthermore, the antioxidant properties of these compounds help mitigate oxidative stress, which is often exacerbated by bacterial activity in the oral cavity. By enhancing the oral microbiome's balance and providing a protective effect against oxidative damage, citrus red leaf extracts present a promising avenue for developing natural preventive strategies against dental caries [8].

2.1.2. Preparation Techniques and Component Changes in Co-fermented Tea

The preparation of co-fermented tea involving citrus red leaf and other plant materials utilizes microbial fermentation processes, primarily employing lactic acid bacteria and yeast. This fermentation enhances the bioavailability of polyphenolic compounds and increases the overall antioxidant capacity of the tea. During fermentation, the microbial activity facilitates the transformation of complex polyphenols into simpler, more bioactive forms, which can be more readily absorbed by the body. Studies have indicated that the fermentation process significantly elevates the levels of catechins and flavonoids, which are crucial for their health-promoting properties. Additionally, the fermentation leads to the generation of new bioactive metabolites that may exhibit synergistic effects, enhancing the tea's overall health benefits. This process not only improves the nutritional profile of the beverage but also contributes to its sensory qualities, making it more palatable. The co-fermentation of citrus red leaf with other botanical ingredients thus represents a valuable method for enhancing the functional properties of tea, potentially leading to more effective oral health interventions [9].

2.1.3. Comprehensive Biological Activity of Citrus Red Leaf Co-fermented Tea Extract

The extract derived from co-fermented tea with citrus red leaf showcases a remarkable synergy of biological activities, including potent antibacterial, antioxidant, and anti-inflammatory effects. In vitro studies have demonstrated that this extract effectively inhibits the growth of various cariogenic bacteria, including Streptococcus mutans and Lactobacillus casei, while exhibiting minimal cytotoxicity to oral mucosal cells. This dual action not only helps in preventing dental caries but also promotes oral mucosal health by maintaining the integrity of epithelial cells. Moreover, the antioxidant capacity of the extract plays a vital role in neutralizing free radicals, thereby reducing oxidative stress in the oral cavity, which is often associated with inflammation and tissue damage. The extract's ability to modulate the oral microbiome further enhances its potential as a therapeutic agent, promoting a balanced microbial environment that supports oral health. Additionally, the extract has shown promise in regulating inflammatory responses, which can be beneficial in managing conditions such as gingivitis and periodontitis. Overall, the co-fermented tea extract represents a multifaceted approach to oral health, combining traditional knowledge with modern scientific insights to create a functional beverage that supports dental care and overall well-being [10].

2.2. The Mechanism of Action of Citrus Red Leaf Fermented Tea Extract in Caries Prevention

2.2.1. Inhibition of Cariogenic Bacteria Growth and Metabolic Activity

Caries is primarily caused by cariogenic bacteria such as Streptococcus mutans, which metabolize sugars to produce acidic byproducts that lead to enamel demineralization. Citrus red leaf fermented tea extract (CRL-FTE) exhibits potent antibacterial properties against these pathogens. The active components within CRL-FTE disrupt the integrity of bacterial cell walls, thereby inhibiting bacterial growth and reducing acid production. Studies have demonstrated that CRL-FTE significantly lowers the metabolic activity of S. mutans, leading to decreased acidogenic potential, which is critical in preventing tooth decay. Furthermore, CRL-FTE has been shown to diminish the biofilm-forming capabilities of cariogenic bacteria, thus reducing their ability to colonize dental surfaces. This reduction in biofilm formation is crucial, as biofilms are protective structures that shield bacteria from host defenses and antimicrobial agents. The extract's efficacy in disrupting biofilm integrity not only supports its role in caries prevention but also highlights its potential as a natural adjunct in oral hygiene products aimed at reducing cariogenic bacterial colonization and subsequent enamel demineralization [11][12].

2.2.2. Inhibition of Plaque Formation and Promotion of Tooth Mineralization

Dental plaque is a significant precursor to caries development, as it provides a habitat for cariogenic bacteria to thrive. CRL-FTE plays a vital role in inhibiting plaque formation by interfering with the adhesion and aggregation of bacterial cells. Research indicates that CRL-FTE can effectively block the initial stages of plaque development by preventing bacterial adherence to tooth surfaces. Additionally, CRL-FTE has been shown to enhance the remineralization of enamel, promoting the deposition of minerals on the tooth surface. This is particularly important in counteracting the effects of demineralization caused by acidic environments. In vitro studies have demonstrated that CRL-FTE promotes the formation of hydroxyapatite crystals, which are essential for enamel repair and strengthening. The extract's ability to facilitate mineral deposition not only combats the effects of cariogenic bacteria but also enhances the overall resilience of teeth against acid attacks, thereby contributing to long-term oral health and reducing the risk of caries [13][14].

2.2.3. Anti-inflammatory and Immune Modulation Effects

Oral inflammation is a critical factor in the progression of dental caries, as it exacerbates tissue damage and facilitates bacterial invasion. CRL-FTE exhibits significant anti-inflammatory properties, which can mitigate the inflammatory response associated with caries development. The extract has been found to downregulate the expression of pro-inflammatory cytokines such as IL-6 and TNF-α, which are often elevated in the presence of cariogenic bacteria. By modulating the immune response, CRL-FTE helps maintain the integrity of the gingival tissue and oral mucosa, thereby

preventing the progression of caries. Moreover, the immune-regulating effects of CRL-FTE support the maintenance of a balanced oral microbiome, promoting the growth of beneficial commensal bacteria while suppressing pathogenic strains. This dual action not only aids in the prevention of caries but also enhances the overall health of the oral cavity, providing a comprehensive approach to caries management [15][16].

2.3. Application Research and Preclinical Prospects of Citrus Red Leaf Fermented Tea Extracts

2.3.1. Progress in In Vitro and Animal Model Studies

In recent years, multiple in vitro experiments have validated the inhibitory effects of Citrus red leaf fermented tea extracts on cariogenic bacteria, highlighting their potential as a natural alternative in dental care. These studies have demonstrated that the extracts possess significant antibacterial properties against Streptococcus mutans, a primary pathogen involved in dental caries development. For instance, the extracts exhibited a marked reduction in bacterial viability and biofilm formation, indicating their effectiveness in disrupting the pathogenic processes associated with tooth decay [17]. Furthermore, the safety profile of these extracts has been established, as they showed minimal cytotoxicity to human oral epithelial cells, suggesting that they can be used safely in oral care products. In addition to in vitro findings, animal model studies have provided compelling evidence of the efficacy of these extracts when administered orally or applied topically. These studies revealed that both methods significantly reduced plaque formation and caries incidence, reinforcing the potential of Citrus red leaf fermented tea extracts as a preventive measure against dental caries [18]. Moreover, research has explored the synergistic effects of these extracts in combination with traditional anti-caries agents, such as fluoride. The findings suggest that the extracts may enhance the cariostatic effects of fluoride, presenting a promising avenue for developing more effective oral care products that leverage both natural and conventional ingredients [19].

2.3.2. Current Status and Challenges in Clinical Research

Despite the promising in vitro and animal model findings, clinical trials involving Citrus red leaf fermented tea extracts remain limited. Preliminary studies indicate that these extracts are safe for oral application and may contribute positively to the oral microbiome, promoting a healthier balance of oral flora [20]. However, the clinical research landscape is hindered by challenges such as small sample sizes and short follow-up periods, which limit the generalizability of the findings. Many studies have not adequately addressed the long-term effects of these extracts on dental health, nor have they established robust methodologies for measuring clinical outcomes related to caries prevention [21]. Furthermore, the existing clinical trials often lack the rigor of larger, multicenter, randomized controlled trials that are necessary to validate the efficacy of these extracts comprehensively. To overcome these challenges, future research must prioritize the design of large-scale clinical trials that can provide definitive evidence of the effectiveness of Citrus red leaf fermented tea extracts in caries prevention. Such studies should also focus on diverse populations to ensure that the findings are applicable across different demographic groups, ultimately paving the way for the integration of these natural extracts into mainstream dental care [22].

2.3.3. Product Development and Application Prospects

Citrus red leaf fermented tea extracts hold significant promise as a natural ingredient in the formulation of dental care products such as toothpaste and mouthwashes. Their demonstrated antibacterial properties and safety profile make them an attractive alternative to synthetic additives commonly used in oral hygiene products. The potential for these extracts to enhance the stability and bioavailability of formulations can be realized through modern pharmaceutical technologies, which can optimize their delivery and effectiveness in oral care applications [23]. The growing consumer demand for green, safe, and effective oral care products aligns perfectly with the market potential for Citrus red leaf fermented tea extracts. As public awareness of the importance of maintaining oral health continues to rise, there is a substantial opportunity for the development of innovative products that incorporate these natural extracts. This aligns with the increasing trend towards holistic health approaches and the use of natural ingredients in personal care products. Furthermore, the incorporation of Citrus red leaf fermented tea extracts into oral care products can meet the rising consumer preference for sustainable and environmentally friendly options, thus enhancing market appeal and consumer trust [24]. As research continues to elucidate the mechanisms through which these extracts exert their beneficial effects, the potential for their application in preventive dentistry will likely expand, contributing to improved oral health outcomes globally.

3. Conclusion

In conclusion, the exploration of the bioactive compounds present in the fermented tea extract from Citrus reticulata leaves reveals a promising avenue for advancing oral health, particularly in the prevention of dental caries. This review has highlighted the multifaceted mechanisms through which this extract exerts its beneficial effects, including significant antibacterial and anti-inflammatory properties, as well as its ability to promote dental mineralization. These findings underscore the extract's potential as a natural caries preventative agent, positioning it as a noteworthy candidate in the realm of dental therapeutics.

The evidence presented from in vitro and animal studies strongly supports the extract's efficacy in inhibiting the growth of cariogenic bacteria and disrupting plaque formation, thereby contributing to a healthier oral microbiome. However, it is crucial to acknowledge the gap that exists between preclinical findings and clinical application. While the laboratory results are promising, the translation of these findings into clinical practice necessitates rigorous human trials to validate the extract's safety and effectiveness in diverse populations.

From an expert perspective, the path forward involves a balanced approach that integrates various research perspectives. Future studies should not only seek to elucidate the specific mechanisms of action of the Citrus reticulata leaf extract but also prioritize the design of well-structured clinical trials. These trials should aim to assess the extract's therapeutic potential in real-world settings, considering factors such as dosage, formulation, and long-term effects on oral health. Moreover, interdisciplinary collaboration among

researchers, dental professionals, and product developers will be essential in advancing this research into marketable dental health products.

Furthermore, the development of innovative formulations that enhance the bioavailability and stability of the active compounds in the extract could significantly improve its practical application. Research should also explore the potential synergistic effects of combining the extract with other natural compounds known for their oral health benefits. This holistic approach could lead to the creation of comprehensive oral care products that not only prevent caries but also promote overall oral health.

In summary, the fermented tea extract from Citrus reticulata leaves holds considerable promise as a safe and effective natural material for caries prevention. By fostering a deeper understanding of its bioactive properties and mechanisms, alongside rigorous clinical validation, we can pave the way for its widespread adoption in dental care. This innovative perspective on caries prevention could not only enhance patient outcomes but also contribute to a paradigm shift in how we approach oral health, emphasizing the importance of natural and holistic solutions in modern dentistry. As we move forward, it is imperative that we remain committed to bridging the gap between laboratory research and clinical application, ensuring that the potential benefits of this promising extract are realized in everyday dental practice.

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